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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,935	05/03/2001	David F. Woodward	D2914	6555

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EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 05/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/847,935	WOODWARD ET AL.	
	Examiner	Art Unit	
	Blessing M. Fubara	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36,37,39-41,43-50,53-66,68 and 70-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36,37,39-41,43-50,53-66,68 and 70-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of amendment filed 02/17/04. Claims 36, 37, 39-41, 43-50, 53-66, 68, 70-86 are pending.

Prostanoid, an efficacy-enhancing component introduced into claim 36 at last amendment is deleted from claim 36 and alpha-2-adrenergic agonist is added to claim 36 by the current amendment.

Claim Rejections - 35 USC § 102

1. The rejection of claims 36, 37, 41, 43, 44, 46-50, 53, 54, 57 and 59 under 35 U.S.C. 102(b) as being anticipated by FR 2272684 (Derwent Database on West) is withdrawn because applicants' argument is persuasive since the FR 2272684 abstract does not disclose alpha-2-adrenergic agonist.

2. The rejection of claims 36, 37, 39-41, 43, 44, 47-50, 53-58, 70-75 and 77 under 35 U.S.C. 102(e) as being anticipated by Garst (US 6,294,563) is withdrawn because claim 36 is amended to recite efficacy enhancing component in amount of greater than 0.2% to less than about 10% and this recited range in amount is not disclosed by Garst.

3. Claim 59 and new claims 78-80 and 83-86 are rejected under 35 U.S.C. 102(e) as being anticipated by Garst (US 6,294,563).

Applicants ague that:

A) Garst does not specifically disclose, teach or suggest a composition that comprises alpha-2-adrenergic agonist therapeutic component and an efficacy-enhancing component provided in an amount of greater than 0.2% (w/v) and less than about 10% (w/v) as recited in claim 36. Applicants further state that the amount of prostaglandin disclosed by Garst in column 8, lines 63 and 64 is less that 0.2%.

B) Garst does not specifically disclose or teach or suggest a composition that comprises an adrenergic agonist and an efficacy-enhancing component provided in a amount that is effective to form ion-pair complex with the adrenergic agonist and which remains intact in a high dielectric constant solvent as recited in claim 59.

C) Regarding claim 74, applicants argue that Garst does not specifically disclose, teach or suggest a composition that includes a linoleic acid component as an efficacy enhancing component.

D) Regarding new claims 78-86, applicants contend that Garst does that disclose, teach or suggest a liquid composition that comprises a therapeutic component a therapeutic component and an efficacy enhancing component provided in an amount effective to form a complex, which is effective to provide a lower or reduced osmotic pressure to the liquid composition relative to a substantially identical composition in which the therapeutic component is not complexed with the efficacy enhancing component.

In light of the above arguments applicant states that the designated claims are not anticipated by Garst under 35 USC 102 and are unobvious from and patentable under 35 USC 103.

Regarding A and B) above, applicants argument is persuasive because the amended claim 36 recites an amount of efficacy enhancing components in the range of greater than 0.2% to less than about 10% and in Garst, the efficacy enhancing component is form about 0.00001 to 0.2 wt%. While Garst does not anticipate claims 36, 37, 39-41, 43, 44, 47-50, 53-58, 70-75 and 77, these claims are obvious over Garst and s rejection under 35 USC 103 will be appropriate.

4. Applicants' arguments filed 02/17/04 have been fully considered but they are not persuasive as the arguments relate to claims 59 and new claims 78-80 and 83-86.

Regarding B as it relates to claim 59) above, Garst discloses a composition that comprises a composition comprising an adrenergic agonist and an efficacy enhancing component. Brominidine is a quinoxaline and an alpha-2-adrenergic agonist and is a 5-bromo-6 (2-imidazolin-2-ylamino) quinoxaline. Prostaglandin is a prostanoid and an efficacy enhancing component. See column 3, line 38; column 4, lines 49-52; column 8, line 60 to column 9 line 10; column 10, lines 1-25, 38-50. It would be expected that a complex would form between the therapeutic component and the efficacy enhancing component and the complex will inherently remain substantially intact in high dielectric constant solvent.

Regarding C) Claim 74 is no longer anticipated by Garst in light of the amendment since claim 74 now recites linoleic acid efficacy enhancing component and Garst does not disclose linoleic acid. Applicants' argument with respect to claim 74 is thus persuasive.

Regarding D) it is respectfully noted that generic claim 78 is directed to a broad liquid composition that contains a therapeutic agent and an efficacy enhancing component and enhancing the pharmakokinetic disposition .... enhancing component is inherent to the composition. Garst specifically discloses a composition that comprises a therapeutic component and efficacy enhancing component and this composition would inherently have the property recited in the instant claim 78. Garst discloses that the composition can be topically applied to an affected eye by applying one or two drops of a liquid composition to the eye (column 10, lines 58-60), and thus Garst discloses a liquid composition.

Therefore, Garst anticipates claims 59, 78-80 and 83-86 and the rejection is reiterated below.

Garst discloses a composition that comprises brimonidine and prostaglandin (column 3, line 38 and column 4, lines 49-52). Garst's composition further comprises vegetable oils, ethyl

cellulose, ethyl oleate, polyvinylpyrrolidone and isopropyl myristate; emulsifying, preserving, wetting or bodying agents (column 10, lines 1-25) or water-soluble polymer carrier (column 10, lines 38-50). Garst further discloses that the composition can contain one or more brimonidine derivatives and one or more prostaglandins (column 8, line 60 to column 9 line 10). Brimonidine is quinoxaline and alpha-2-adrenergic agonist and is a 5-bromo-6 (2-imidazolin-2-ylamino) quinoxaline. Prostaglandin is a prostanoid. No amounts and/or conditions were recited in the instant claims that would allow the composition of the application to form a complex and exclude the same composition in the prior art from forming a complex. The property of a composition cannot be separated from the composition. The teaching of Garst meets the limitations of the claims.

5. The rejection of claims 60-66, 68, 72 and 73 under 35 U.S.C. 102(e) as being anticipated by Gil et al. (US 6,294,553 is withdrawn because Gil does not disclose amounts of efficacy enhancing component as recited in the generic claim. While applicants' argument as it regards to Gil and claims 60-66, 68, 72 and 73 is persuasive as it regards the amount of the efficacy enhancing components, claim 74 which recites linoleic acid component as the efficacy enhancing component was not rejected under 35 USC 102 over Gil. Thus with respect to this side of the argument, applicants are not persuasive. However, these claims are obvious over Gil and the rejection will be presented below under 35 USC 103.

6. New claims 78-86 are rejected under 35 U.S.C. 102(e) as being anticipated by Gil et al. (US 6,294, 553).

Applicants argue that Gil does not disclose, teach or suggest a composition that comprises a therapeutic component and an efficacy enhancing component that is provided in an amount effective to form a complex, which is effective to provide a lower or reduced

osmotic pressure to the liquid composition in which the therapeutic component is not complexed with the efficacy enhancing component.

7. Applicants' arguments filed 02/17/04 have been fully considered but they are not persuasive.

Claim 78 is a broad teaching of a composition that comprises a therapeutic component and an efficacy enhancing component. No amounts and/or conditions were recited that would allow the composition of the application to form a complex and exclude the same composition in the prior art from forming a complex.

Gil discloses a composition that comprises brimonidine, which is a 5-bromo-6 (2-imidazolin-2-ylamino) quinoxaline and an alpha-2-agonist (abstract, column 2, lines 50 and 61,column 3, lines 12, and 37-39), oleic acid or anionic surfactant (column 4, lines 20-22), buffers (column 4, lines 28-37), physiological saline solution and vehicles such as poloxamers and cellulose polymers (column 4, lines 4-10); the composition of Gil is a solution or liquid applicable as an ophthalmic with a physiological saline solution as the vehicle and where the pH of the ophthalmic is between 6.5 and 7.2 (column 3, lines 65-67). Oleic acid is a fatty acid. The anionic surfactants are generally polymers. Effective amount is any amount. A pH of 7.2 is greater than 7 and lies between 7 and 9. Nothing in applicants' composition indicates that a complex would not form in the composition of the cited references. In the present case, it is a broad composition where therapeutic agent forms a complex with efficacy enhancing component. In this case the prior art teaches a composition comprising a therapeutic component and efficacy enhancing component; and the examined claims are directed to a composition comprising a therapeutic component and efficacy enhancing component. The teaching of Gil meets the limitations of the claims.

Claim Rejections - 35 USC § 103

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

9. Claims 36, 37, 39-41, 43, 44, 47-50, 53-58, 70-75 and 77 rejected under 35 U.S.C. 103(a) as being unpatentable over Garst (US 6,294,563).

Garst discloses a composition that comprises brimonidine and prostaglandin (column 3, line 38 and column 4, lines 49-52). Garst's composition further comprises vegetable oils, ethyl cellulose, ethyl oleate, polyvinylpyrrolidone and isopropyl myristate; emulsifying, preserving, wetting or bodying agents (column 10, lines 1-25) or water-soluble polymer carrier (column 10, lines 38-50). Garst further discloses that the composition can contain one or more brimonidine derivatives and one or more prostaglandins (column 8, line 60 to column 9 line 10). Brimonidine is quinoxaline and alpha-2-adrenergic agonist and is a 5-bromo-6 (2-imidazolin-2-ylamino) quinoxaline. The amount of prostaglandin in Garst's composition is between about 0.00001 and about 0.2 wt% (column 8, lines 63 and 64); and prostaglandin, which is an efficacy enhancing component is also a prostanoid.

Garst thus discloses the instant composition. The difference between Garst and the instant composition is in the amount of the efficacy enhancing component. While the efficacy enhancing component in the instant claims is greater than 0.2% for the lower limiting amount, the amount of the efficacy enhancing component in Garst is at about 0.2% for the upper limit. However, differences in concentration/amounts will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration/amount is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller,

220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Secondly, there is no demonstration in applicants' specification showing that efficacy enhancing component in amounts greater than 0.2% and less than 10% provides unusual results. The burden is on applicants to demonstrate such is the case.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the composition of Garst that comprises a therapeutic agent and prostaglandin in amounts of about 0.2%. One having ordinary skill in the art would have been motivated to optimize the composition of Garst by including amounts of prostaglandin and therapeutic agents that would be expected to effectively reduce or control intaocular pressure (IOP).

10. Claims 60-66, 68, 72, 73 and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gil et al. (US 6,294,553).

Gil discloses a composition that comprises brimonidine, which is a 5-bromo-6 (2-imidazolin-2-ylamino) quinoxaline and an alpha-2-agonist (abstract, column 2, lines 50 and 61,column 3, lines 12, and 37-39), oleic acid or anionic surfactant (column 4, lines 20-22), buffers (column 4, lines 28-37), physiological saline solution and vehicles such as poloxamers and cellulose polymers (column 4, lines 4-10); the composition of Gil is applicable as an ophthalmic with a physiological saline solution as the vehicle and where the pH of the ophthalmic is between 6.5 and 7.2 (column 3, lines 65-67). Oleic acid is a fatty acid. The anionic surfactants are generally polymers. Effective amount is any amount. A pH of 7.2 is greater than 7 and lies between 7 and 9. Nothing in applicants' composition indicates that a complex would not form in the composition of the cited references. In the present case, it is a broad composition where therapeutic agent forms a complex with efficacy enhancing component. In this case the prior art

teaches a composition comprising a therapeutic component and efficacy enhancing component; and the examined claims are directed to a composition comprising a therapeutic component and efficacy enhancing component. The teaching of Gil meets the limitations of the claims.

Gil thus discloses the instant composition. The difference between Gil and the instant composition is that Gil is silent in the amount of the efficacy enhancing component. While the efficacy enhancing component in the instant claims is greater than 0.2% for the lower limiting amount, the amount of the efficacy enhancing component in Gil does not indicate how much efficacy enhancing component should be used in the composition. However, differences in concentration/amounts will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration/amount is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Secondly, there is no demonstration in applicants' specification showing that efficacy enhancing component in amounts greater than 0.2% and less than 10% provides unusual results. Also, since Gil is silent on the amount of the efficacy enhancing component, it would appear that all or certain amount of the efficacy enhancing component would be suitable to provide the desired effect and it is within the purview of the person of skill or of ordinary skill to determine the workable amount of the efficacy enhancing component. The burden is on applicants to demonstrate such is the case.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the composition of Gil that comprises a therapeutic agent and anionic polymer. One having ordinary skill in the art would have been motivated to optimize the

composition of Gill by including appropriate amount of anionic surfactant and therapeutic agents in a composition that would be expected to effectively treat ocular pain.

11. The rejection of claims 45 and 76 under 35 U.S.C. 103(a) as being unpatentable over Garst (US 6,294,563) and Dean et al. (6,242,442) is not maintained because neither Garst nor Dean discloses docosahexanoic acid in the composition.

A new rejection is made it its place.

12. Claims 36, 45 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shashoua et al. (US 5,795,909).

The generic claim is directed to a composition that comprises alpha-2-adrenergic agonist as the therapeutic agent and greater than 0.2% to about less than 10% efficacy enhancing component. The rest of the claim bears no patentable weight to the claimed invention.

Shashoua discloses a composition that contains Brimonidine tartrate (column 20, line 48), which is quinoxaline and alpha-2-adrenergic agonist, and conjugated C22 unbranched carbon chain (column 3, line 55). In this case the conjugated unbranched C22 carbon chain is cis-docosahexanoic acid. Linoleic acid and linolenic acid are all conjugated unbranched unsaturated acids that can substitute for docosahexanoic acids in pharmaceutical compositions. Thus regarding claim 46, docosahexanoic acid can be substituted for by linoleic acid with the expectation of maintaining the effectiveness of the brimonidine as quinoxaline and alpha-2-adrenergic agonist.

The difference between Shashoua and the instant claim is that Shashoua does not disclose amounts of the fatty acid in the pharmaceutical. However, differences in concentration/amounts will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration/amount is critical. "[W]here the general conditions of a

claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Secondly, there is no demonstration in applicants' specification showing that efficacy enhancing component in amounts greater than 0.2% and less than 10% provides unusual results. Also, since Shashoua is silent on the amount of the efficacy enhancing component, it would appear that all or certain amount of the efficacy enhancing component would be suitable to provide the desired effect and it is within the purview of the person of skill or of ordinary skill to determine the workable amount of the efficacy enhancing component. The burden is on applicants to demonstrate such is the case.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the composition of Shashoua that comprises a therapeutic agent and a conjugated unsaturated fatty acid. One having ordinary skill in the art would have been motivated to optimize the composition of Shashoua by including appropriate amount of the conjugated unsaturated fatty acid and therapeutic agents in a composition that would be expected to effectively treat mammalian cell proliferative disorder.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 242-0594. The examiner can normally be reached on 7 a.m. to 3:30 p.m. (Monday to Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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